McCune-Albright Syndrome (Fibrous Dysplasia) Associated with an Orbital Tumor

DAVID SEVEL, MD, PHD, HECTOR E. JAMES, MD, RICHARD BURNS, MD, AND KENNETH LEE JONES, MD

Craniofacial fibrous dysplasia has rarely been described in the polyostotic form of McCune-Albright disease. The unique ophthalmic features of interest in this patient with McCune-Albright's disease was the presence of an orbital tumor that suddenly increased in size compressing the optic nerve. Prompt excision of the tumor resulted in restoration to normal vision.

The McCune-Albright (M-A) syndrome, as originally described in young girls, consisted of polyostotic fibrous dysplasia of the skeleton, large café-au-lait spots, and precocious puberty. While unilateral proptosis[1-6] has been described in fibrous dysplasia of the orbital bones it has only rarely been recorded in the McCune-Albright syndrome. Subsequent experience with the condition has revealed that males are also affected, though less often, and that endocrinopathies other than precocious puberty occur. It is also recognized that the skeletal dysplasia can occur with either endocrinopathy or cutaneous pigmentation as well as with the full triad. Though the endocrine manifestations have been the most extensively investigated and are the most controversial, the skeletal disorder is usually the most disabling and the source of ophthalmologic complications.

Report of a Case

The patient first presented to the University of California, San Diego Medical Center at the age of 1 and 11/12 years with a history of vaginal bleeding. She had been born at term, following an uncomplicated pregnancy, weighing 7 lb 7 ounces and had been noted at birth to have multiple "birthmarks" which were thought to have lightened with age. At 1 and 9/12 years she developed a brownish vaginal discharge which progressed to frank vagina bleeding. Approximately two months later there was a five-day span of vaginal bleeding, following which she was evaluated at the UCSD Medical Center. Physical examination at that time revealed many large, irregular café-au-lait spots over the trunk and extremities. Five centimeters of breast tissue were palpated bilaterally and areolar widening was noted. A few pubic hairs were present over the mons and labia majora. Skeletal x-rays revealed changes characteristic of polyostotic fibrous dysplasia in the long bones and skull. The right hip and femur were most extensively involved (Fig 1).

At this admission, pituitary function was studied with infusions of arginine,[7] thyrotropin releasing hormone (TRH),[8] and gonadotropin releasing hormone (GnRH).[9] All responses were normal with the luteinizing hormone (LH0 and follicle stimulating hormone (FSH) responses to GnRH being prepubertal in pattern (unpublished data). At the age of 2½ years, the gonadotropin secretion through sleep was studied with no significantly elevated levels (unpublished data). One month later, in view of her progressive sexual development and repeated episodes of vaginal bleeding, treatment was initiated with medroxyprogesterone at a dose of 100 mg intramuscularly, every two weeks. This successfully arrested her menses and breast development. She continued on the medication for 3 and 9½ years with continued acceleration of growth and bone age with no progress in sexual development. During this time recurrent long bone fractures occurred. These especially involved the right femur. She required multiple

From the University of California, San Diego, California.

Reprint requests to University Hospital (H-898), 225 Dickinson St, San Diego, CA 92103 (David Sevel, MD, PhD).

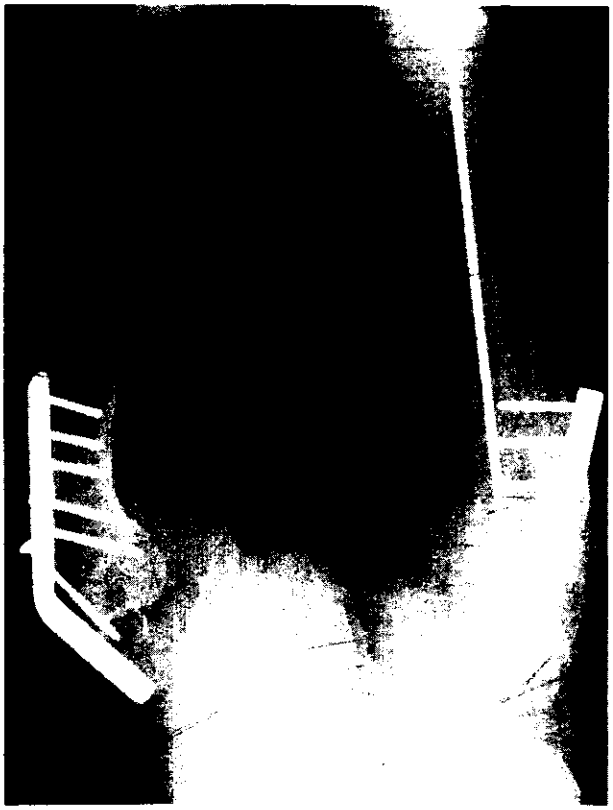

Figure 1 There is pelvic deformity consisting of medial movement of right hemipelvis. Bony structures are generally expanded and demineralized. There is bilateral hip nailing with blade-plate prosthesis and a right femoral intramedullary rod is present in the femoral shaft.

correction surgical procedures and eventually had both femurs fixed with intramedullary rods (Fig 1).

The medroxyprogesterone regimen was discontinued at age 6 and 3/12 years and she reinitiated her pubertal develoment with regular menses. She was followed regularly and progressed to Tanner IV breasts and pubic hair by age 8 and 8/12 years. During a routine evaluation she was noted to be developing prominence of her right eye. Thyroid function studies at this time were normal.

The patient was first seen in May 1980, at the age of 8 years, in the Ophthalmology Clinic at the University of California, San Diego. At this time the patient had a right proptosis of six months' duration. She had no previous history of eye problems and denied any ocular complaints. The visual acuity without correction was 20/20 -2 in the right eye and 20/20 in the left eye. The pupils were equal in size and reacted briskly to direct and consensual light stimulation as well as to accommodation and a Marcus-Gunn pupil was not demonstrable. Extraocular movements were full in all directions of gaze. Exophthalmometry (Hertel) reading set at 95 mm revealed the right eye to be proptosed to 17 mm as compared with 14 mm on the left side. No masses were palpated in the orbit and the right eye was retropulsed without resistance. No bruit was auscultated, and the proptosis did not increase with the Valsalva maneuver. Slit-lamp examination showed mild punctate staining of the inferior aspect of the right cornea. Examination of the fundi showed pink disks whose edges were well-defined. There was no venous congestion/or arteriovenous nipping. Neither retinal edema nor hemorrhages were noted in the retinal background. Visual field examination with the Goldmann perimeter was normal in both eyes. A series of x-rays of the skull revealed fibrous dysplasia of the greater wing of the right sphenoid as well as the right temporal bone. As a distinct mass was not demonstrable, and vision was unaffected, it was decided that surgical exploration of the orbit was not indicated. Computerized axial tomography done on June 24, 1980, showed the brain parenchyma to be normal. With the appropriate window setting the skull was studied and found to be thickened in the area of the right sphenoid wing, with a splintering effect in that region and the back of the right orbit. A soft tissue density was seen in the area of the right frontal sinus and right supraorbital region, within the bone of the right frontal area.

The proptosis that was noted on clinical findings was present on the CT scan, and the optic nerve was clearly seen on the right. The left orbit appeared normal.

The patient was free of ocular symptoms until September 1981 at which time the mother noticed increased tearing from the right eye. Despite denying visual symptoms other than the tearing, the visual activity of the right eye was noted to be 20/50 improving to 20/30+ with a pinhole. The visual acuity of the left eye remained at 20/20. Applanation tonometry was 14 mm Hg in the right and 18 mm Hg in the left. Pupils were equal in size, round, and reacted to direct and consensual light stimulation and again a Marcus-Gunn pupil was not demonstrable. Extraocular movements were full in all directions of gaze. The Hertel exophthalmometry readings, set at 95 mm, were 23.5 on the right eye and 16 mm on the left eye (Fig 2). A firm mass was palpable in the right orbit. It was approximately 25 mx 15 ms 9.5 mms. It was firm, and the edges were well-defined

Figure 2 Right eye is proptosed inferomedially due to a mass in the superolateral aspect of the orbit.

inferiorly, laterally, and medially but the superior border could not be identified as it extended inferior to the supra-orbital margin. The mass was not compressible and a bruit was not heard either in the region of the mass, over the overlying bone, or in the region of the carotid artery on the right side. The tumor was nontender, the overlying skin was not inflamed, and was not adherent to it (Fig 3). Examination of the fundi showed the disks to be pink and the edges were well-defined. There was minimal venous congestion present but no retinal edema was noted. At the 12 o'clock position of the fundus a mass was noted to indent the eye, and this was accentuated when the eye was elevated. Extaocular movements were full in all directions of gaze except in elevation where there was some decreased movement particularly in the extremes of gaze. Questionable diplopia was noted in elevation. There was minimal conjunctival injection on the right but diffuse punctate staining of the inferior cornea was noted.

On Oct 6, 1981, transocular B scan of the right eye aiming at the 12 o'clock equator from the lower lid, revealed a mass with low reflectivity indenting the eye superiorly. B scan of the right supraorbital paraocular region at 12 o'clock disclosed a mass starting just behind the skin with a sharp posterior wall (Fig 4).

Figure 3 Mass is located just inferior to the supra-orbital ridge and its surface is smooth and causes skin of upper lid to bow forward (arrowed). Eye is markedly proptosed.

Transocular A scan of the right eye aiming at the 12 o'clock position from the inferior sclera disclosed a mass lesion of low refectivity (20%-40%) approximately 17 mm in depth with evidence of a defect in the bony roof superiorly. The lesion was not compressible though the eye was paraocular just behind the skin and ending with a sharp border and a high refectivity peak approximately 31 mm behind the skin (Fig 5).

On Oct 1, 1981 a high resolution CT scan was performed of the brain, anterior frontal fossa, and orbits. There was a soft tissue density mass which had eroded the sphenoidal wing on the right side and had protruded into the right anterior cranial fossa (Fig 6 and 7) and destroyed the right supra-orbital rim. In the right orbit a mass had caused gross forward displacement of the right globe and extended into the apex of the orbit and compressed the optic nerve which could not be visualized (Fig 8). Within the orbit a finger-like projection was noted in the lateral aspect of the orbit. The tissue density of the mass was similar to that of brain parenchyma but enchanced in a patchy fashion with contrast. There was no blunting or distortion of the right or left lateral ventricles.

On Oct 7, 1981, the patient returned to the Ophthalmic Clinic complaining of right frontal headaches. There was mild erythema and tenderness over the right supra-orbital ridge. The pupils were equal in size and reacted to direct and consensual light stimulation. A Marcus-Gunn pupil was not demonstrable. However,

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Figure 4 Transocular B scan of the orbital mass demonstrates a sharp posterior wall (arrowed). There are foci of reflectivity within the substance of the tumor.

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exophthalmometer reading showed progression of the proptosis of the right eye to 28 mm compared to 16 mm of the left eye. The visual acuity was decreased in the right eye to 20/40 -1 while that of the left eye remained 20/20. The mass indented the globe from above. The rest of the ophthalmic examination was essentially unchanged from that of Nov 30, 1981.

In the light of new findings, neurosurgical opinion (H.J.) was obtained, and a joint neurosurgical/ophthalmic procedure was scheduled to take place on Oct 14, 1981.

On Oct 11, 1981, the patient presented to the Emergency Room with severe pain and photophobia over the right eye. The visual acuity in the right eye had deteriorated to perception of hand motion. The right eye was markedly proptosed inferolaterally. Ocular movements were restricted in all fields of gaze. There was gross corneal exposure such that direct ophthalmoscopy of the fundus was not possible. A positive Marcus-Gunn pupillary reflex was noted on the right side. The patient was admitted to the hospital, and arrangements made for surgical exploration.

Following endotracheal intubation, the patient was prepared and draped in the standard fashion for a bicoronal incision with the head slightly rotated to the left for an adequate exposure of the right frontal region. A bicoronal incision was performed and almost immediately, a vascular, soft fleshy mass was observed to protrude through the supraorbital area and the supraorbital rim. This mass was dissected off the adjacent bone. In order to gain access intracranially, it was necessary to do a right frontal craniotomy. The bone was found to be extremely soft, thickened, and vascular. Once the frontal bone flap was elevated, the dura was noted to be indented by the mass that was located in the supraorbital region. While there were areas of adherence of the mass to the dura but no penetration of the dura was noted. With difficulty, the mass was dissected from the dura. The mass extended through the orbital roof anteriorly into the orbital cavity. The frontal lobe was retracted extradurally, and the orbital roof opening expanded with rongeurs. The tumor could be seen extending posteriorly into the orbit and displacing the eye

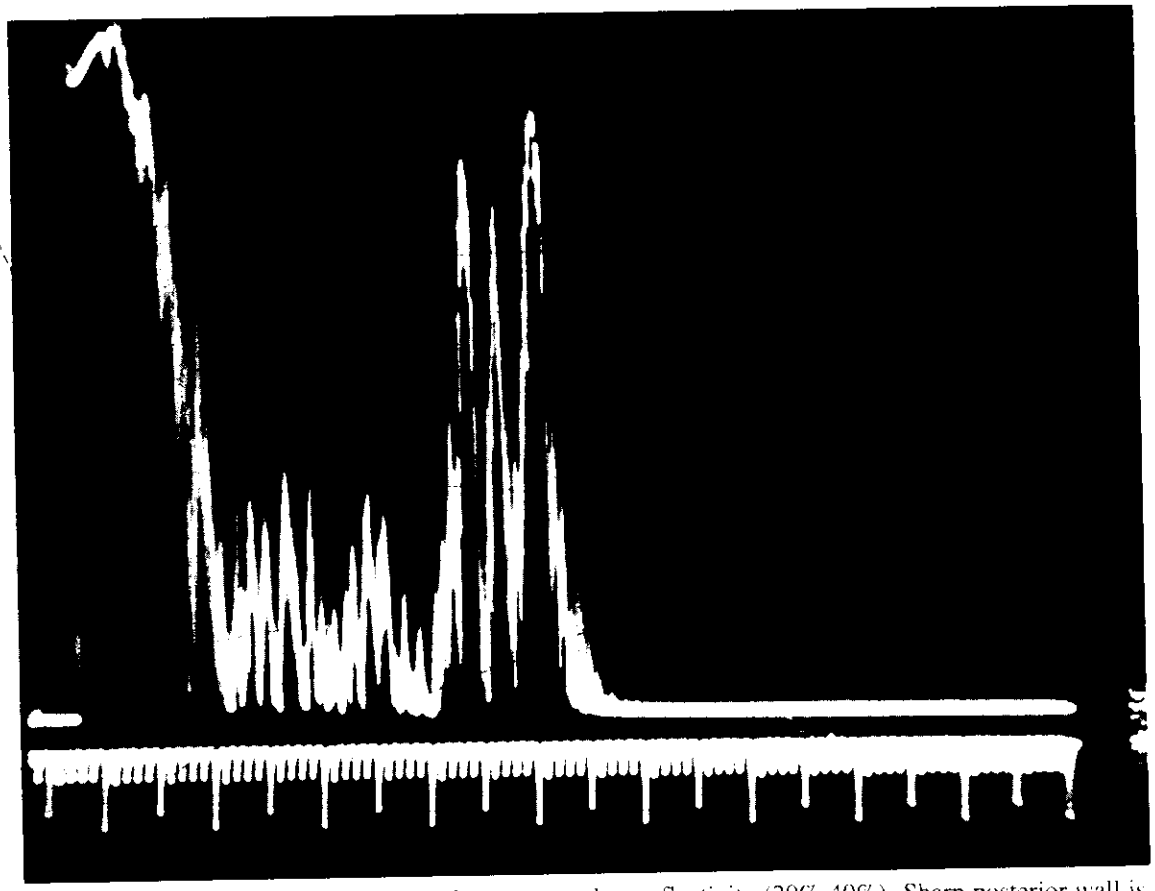

Figure 5 Transocular A scan of orbital mass demonstrates low reflectivity (20%-40%). Sharp posterior wall is again noted.

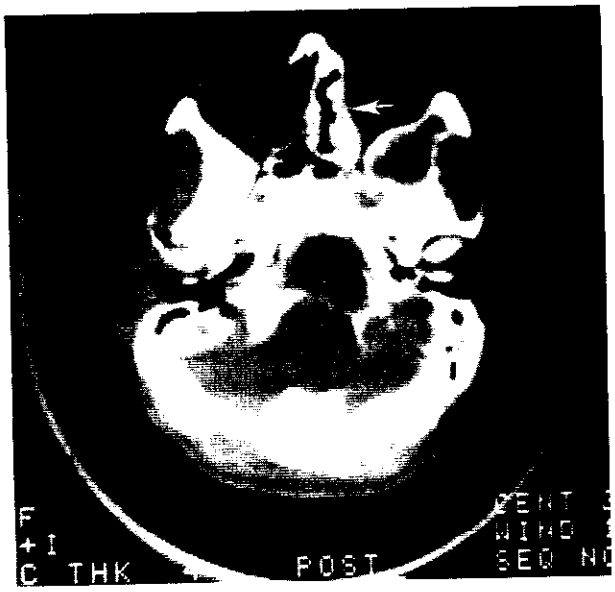

Figure 6 CAT scan (coronal view) shows soft tissue tumor causing ? compression ? invasion of the ethmoidal sinus (arrowed) and proptosis of the right eye.

inferiorly and anteriorly. Extensive hemorrhage was encountered that was controlled with difficulty in the manipulation of the tissue. The supraorbital and frontal component of the mass was excised.

The orbital exploration (D.S.) revealed the main vascular tumor to be approximately 5 cm by 5 cm. It was extremely hemorrhagic and soft; its edges were ill-defined and the mass was not encapsulated. The tumor was gently dissected off the periobita in a distinct plane of cleavage between the tumor and the levator palpebrae superioris muscle. There were three extensions to the main tumor mass. One extended laterally in the direction of the lacrimal gland. This was easily dissected off the underlying levator palpebrae superioris muscle. The second limb of the tumor extended medially. It was noted that the medial wall of the orbit was absent and the mucosa of the ethmoidal sinus was discernable. With meticulous dissection, this extension of the mass was excised (Gelfoam packs were used to stem the bleeding). A further limb of the tumor was directed posteriorly in the direction of the superior orbital fissure. It was deemed, at this stage, inadvisable to dissect the tumor posteriorly as the

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integrity of the optic nerve and the structures passing through the superior orbital fissure, would be in jeopardy.

A portion of the diseased frontal bone was then used as a bone strut over the roof of the orbit so as to reconstruct the roof of the orbit. The rest of the frontal bone was used to realign the supraorbital region. The skin and galea were approximately closed.

Histological examination indicated thickening of the trabeculae of the surrounding normal bone, presumably a reaction to the fibrous tissue which had infiltrated the bone. Trabeculation of bone and lamellar lines were not noted, but coarse woven bone was observed (Fig 9). Osteoblasts were not present at the margins of the trabeculae, and the stroma was only moderately cellular. The trabeculae tended to merge with the fibrous cellular component. In addition, there was a large amount of somewhat bloody, loosely arranged fibrous tissue with giant cells (Fig 10).

Postoperative Progress

On Oct 12, 1981, twelve hours after surgery, the eyelids were moderately swollen. The eye was less proptotic although no reading with the Hertel Exophthalmometer was possible. The patient was able to count fingers at 2 ft with the right eye. Extraocular movements revealed minimal ability to elevate the eye although it was not possible to determine how much of this was due to the swelling and congestion from the surgery. The fundus was not clearly seen because of ophthalmic ointment.

On Oct 14, 1981, the visual acuity was 20/50 -2 with the hand held Snellen's chart. There was minimal proptosis and the cornea was protected by the eyelid. A subconjunctival hemorrhage was present. The cornea had a slight haze, most likely a resultant of the exposure keratitis. Extraocular movements still had some limitation in elevation. There was a questionable Marcus-Gunn pupil. The fundus exam revealed a sharp, well-defined pink disc with normal vessels, background and macula.

On Oct 15, 1981, the visual acuity was 20/50+. Again there was minimal proptosis. The patient was noted to be able to elevate her eye slightly. The subconjunctival hemorrhage was still present and mild corneal haze was noted. The patient was discharged on Oct 16 with these same ophthalmic findings.

On Oct 21 she was reassessed in the Ophthalmic Clinic. The visual acuity of the right eye was 20/40. Minimal proptosis without a pulsating component was noted.

On Oct 23, 1981, the distance visual acuity had improved to 20/40 without correction and

Figure 7 CAT scan (sagittal view) shows extension of soft tissue tumor through the roof of orbit into anterior cranial fossa (arrowed).

Figure 8 CAT scan (coronal view) shows erosion (arrowed) of the roof of the orbit by the soft tissue tumor.

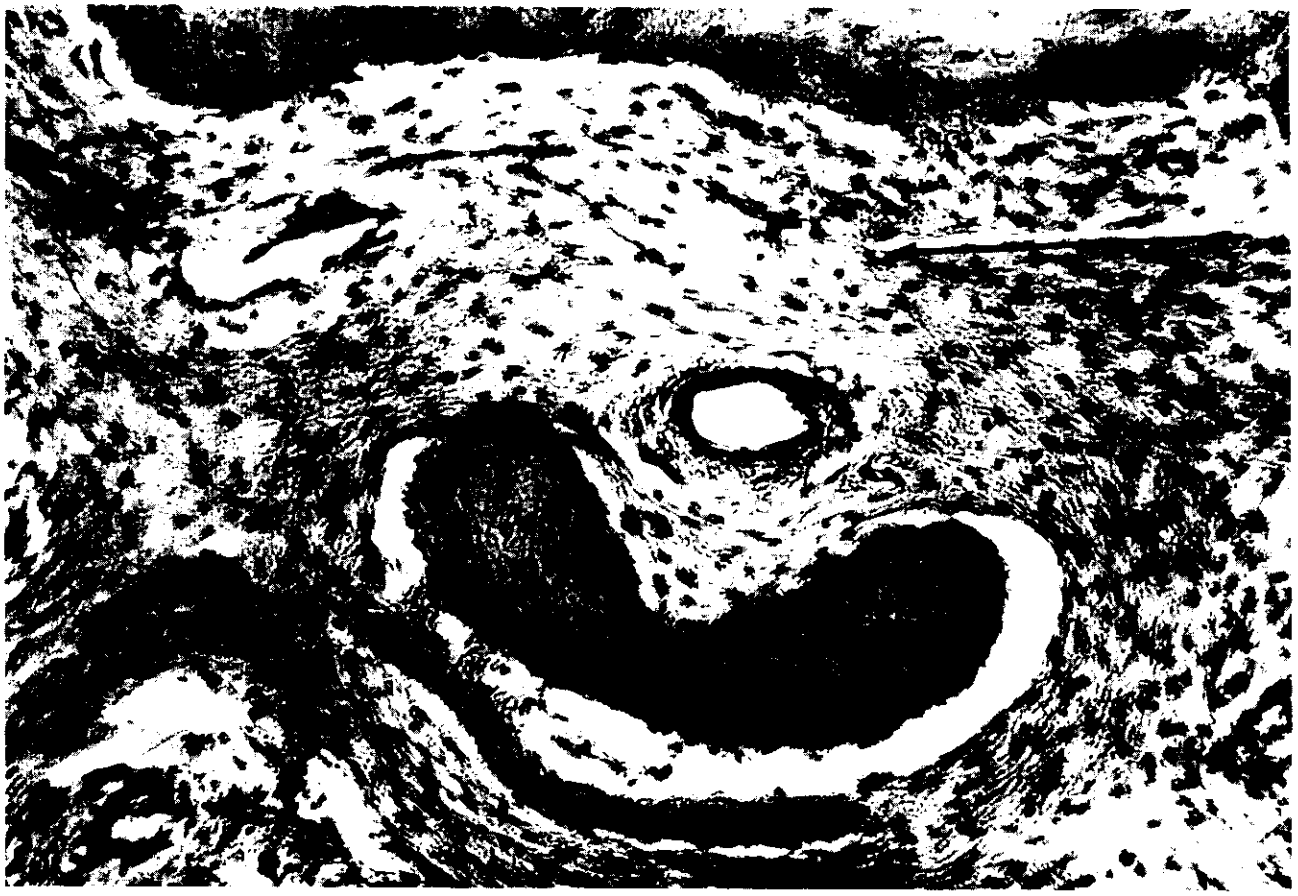

Figure 9 Bone is infiltrated by loosely arranged fibrous cellular tissue (arrow). (hematoxylin and eosin, ×40).

20/30 with a pinhole. The vision of the left eye was 20/20. Superficial punctate keratopathy and a few subepithelial opacities were noted but were not located in the visual axis. Hertel exophthalmometer readings set at 95 mm revealed the right eye to be proptosed at 21 mm as compared to the left eye at 17 mm. There was full extraocular muscle mobility. The pupils were equal and reacted briskly. There was no Marcus-Gunn pupil. The fundus examination was entirely withing normal limits and there was no optic atrophy.

The patient was next seen on Nov 20, 1981. The visual acuity of the right eye was 20/20 - 3 and 20/20 in the left eye. The pupillary reflexes were intact and there was no Marcus-Gunn pupil. She had full mobility of her extraocular movements. She again had temporally located subepithelial opacities of her cornea. The fundus exam was entirely within normal limits, without evidence of optic atrophy. A visual field examination was entirely normal. The reconstructed supraorbital and frontal region achieved a very satisfactory cosmetic result. In view of this remarkably rapid return of vision, the patient was discharged from the Ophthalmology Clinic and is not scheduled to be seen for another three months. The patient is also being followed in the Neurosurgery and Orthopedic divisions at UCSD.

Discussion

The ophthalmic features of interest in this case were two-fold. The ocular complications of craniofacial fibrous dysplasia occur more frequently with the monostotic and indeed are rare with the polyostotic form.[10-11]

Secondly, the clinical presentation of this case is unique. While large masses have been noted in the orbit,[12] the rapid growth of a small nodule that had a predilection for growing inferolaterally and compressing the optic nerve has not been recorded in the literature. The explosive enlargement of the tumorous mass was due to a hemorrhage in its substance sufficient to compress the optic nerve (resulting in a visual acuity of light perception) and also causing severe exposure keratopathy. There was no evidence of a sphenoidal mucocele to account for the sudden loss of vision.[12] It was initially sus-

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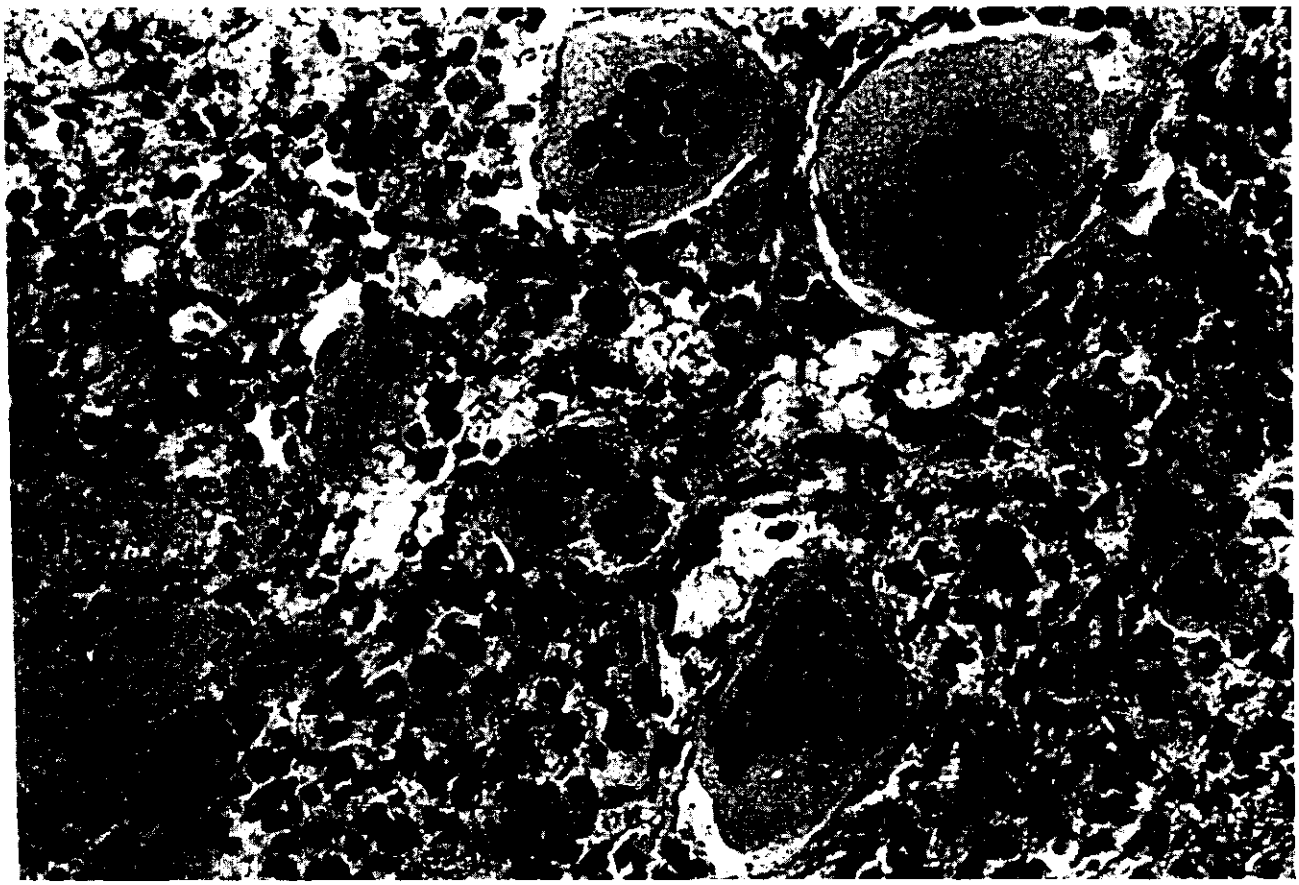

Figure 10 Giant cells are present in the hemorrhagic fibrous tissue component of the tumor (hematoxylin and eosin, ×200).

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pected that this rapid growth of the tumor was due to a malignant transformation, eg, osteosarcoma.[13-17] While a case of recurrent hemorrhage into an area of cranial fibrous dysplasia has been described,[18] there was no danger to vision. A further unique feature of this case was the dramatic reversal of the symptomatology following surgery.

In addition to the unusual ocular symptoms, the patient's clinical course illustrates many common features of this disease.

The etiology of the endocrine disturbance in this disease complex is unclear. In addition to isosexual precocity and hyperthyroidism, hyperadrenocorticism,[19,20] acromegaly[21] and gigantism,[22,23] hyperparathyroidism,[24] and hyperprolactinemia[25] have been reported.

One theory concerning the cause suggests that there is a hypersecretion of one or more hypothalamic releasing hormones.[26] Though this proposal would adequately explain hypersecretion of growth hormone and some cases of precocious puberty, it would not account for the occurrence of hyperparathyroidism. The absence of increased levels of TSH in patients with hyperthyroidism,[27,28] and ACTH in patients with Cushing's disease[20] also argues against this theory.

A second hypothesis suggests that the involved end organs are especially sensitive to trophic hormones or that they function autonomously.[29] The multinodular goiters in M-A patients with hyperthyroidism[28] and nodular adrenal hyperplasia[20] seen with Cushing's syndrome and M-A syndrome argue, in the minds of some investigators, for autonomous hyperfunction.

Neither theory completely explains the endocrine findings in all of the patients observed. It may be that these are a variety of etiologies or that the syndrome represents a third type of multiple endocrine adenomatosis as suggested by DiGeorge.[30]

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